

HEALTH RESEARCH GROUP
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 WASHINGTON, D. C. 20036
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EXECUTIVE SECRETARIAT Food and Drug Administration			
Routing	Action	Info	Coord
HFC-10	✓		
Schmidt		✓	
Mr. Gardner		✓	
February 21, 1974		<input type="checkbox"/> Direct Reply	
<input type="checkbox"/> Prepare for Signature of:			
Remarks: Direct			

February 21, 1974

Dr. Alexander M. Schmidt, Commissioner
 Food and Drug Administration
 5600 Fishers Lane
 Rockville, Maryland 20852

Dear Dr. Schmidt:

As you know, a rapidly rising number of cases of liver cancer (angiosarcoma) are being discovered in workers exposed to vinyl chloride. Combined with other human evidence of liver disease, an earlier study showing cancer in animals, and a recent study in animals demonstrating carcinogenicity with exposures as low as 250 parts per million, it appears that another common chemical has joined the growing list of environmental carcinogens.

Although the major use of vinyl chloride monomer is to make polyvinyl chloride (PVC), several percent of the billions of pounds of vinyl chloride manufactured each year goes into the production of other goods.

We have learned that a significant amount of vinyl chloride is used as an aerosol propellant in consumer products including hair sprays. According to one published report (Aerosol Age, April 1964, p. 47), the levels of vinyl chloride, under conditions where hair spray was being used, can exceed 250 parts per million. (See petition, p. 2)

Several requests for action are detailed in the attached petition. In addition, we request that you make public the brand names of all aerosol cosmetic products presently marketed or marketed at any time in the past which contain vinyl chloride as a propellant. When matters of health and grave danger are at stake, the public has the right to be fully informed about the dangers it faces or has faced from using particular brand name products--regardless of the public relations damage that certain companies may suffer. All those people who have been exposed at any time to products containing vinyl chloride should be made aware of this so that they can inform their physicians.

Thank you for your consideration.

Sincerely yours,

Andrea M. Hricko *Sid Wolfe, M.D.* **CPI**
 Andrea M. Hricko Sidney W. Wolfe, M.D.

74P-0001

Vinyl chloride monomer is a colorless gas which can cause acute toxicity manifested by dizziness, headache, disorientation, and unconsciousness at high concentrations. It has been linked to osteolytic (bone destructive) lesions of the hands, liver disease, and liver cancer in workers engaged in the polymerisation of polyvinyl chlorida from vinyl chloride monomer. In one study of industrial workers exposed to vinyl chlorida 30% were found to have liver enlargement. At exposure levels as low as 250 ppm, vinyl chloride has produced liver cancer in rats. Of greatest significance, since 1964 five workers engaged in making polyvinyl chloride from vinyl chloride monomer at one plant have died from a rare and invariably fatal form of cancer of the liver. The most recent death was December 19, 1973. This cancer has recently been diagnosed in a sixth worker in the same plant.

IV. The Use or Presence of Vinyl Chlorida in Cosmetic Products

Vinyl chloride is among the most often-used propellants in aerosols (Postgraduate Medicine, p. 65; Report of the Committee on Aerosol Toxicity, p. 19.), and is a propellant in hairsprays (Aerosol Age, p. 47 and an industry source, January, 1974.) A 1964 report estimated that spraying hairspray in a tiny room of 282.5 cubic feet for 30 seconds would result in 0.025% vinyl chloride by volume (Aerosol Age, p. 47). This level would correspond to over 250 ppm vinyl chloride in the air of a room that size,³ not unlike the size of many bathrooms in small apartments.

Polyvinyl chloride (PVC) is produced by the polymerisation of vinyl chloride. About 46 million pounds of PVC were used in plastic bottles in 1970. Plastic bottles (PVC and polyethylene together) comprise about 35% of the toiletries and cosmetics

³Using Aerosol Age's reference that 16.5% by volume corresponds to 460 g. vinyl chloride/M³, and a conversion factor of 500 ppm = 1300 ug/M³.

packaging market (Chemical and Engineering News, April 12, 1971, p. 22).

After the manufacture of PVC, about 500 to 3000 ppm of vinyl chloride is entrapped in the PVC resin (Statement of Sheldon Samuels, February 15, 1974). The vinyl chloride monomer--in FDA's own tests--has been found to migrate out of PVC containers into the alcoholic beverages they contain. (See following discussion). To our knowledge, no tests have been conducted to determine whether other alcohol or organic solvent-containing liquids (e.g., bath lotion or perfume can also leach detectable amounts of vinyl chloride from their polyvinyl chloride containers.

V. Prior Regulatory Actions on Vinyl Chloride

1971. In 1971 under Section 6(a) of the Occupational Safety and Health Act of 1970, the Department of Labor adopted as a Federal standard a ceiling level of 500 ppm (1300 mg/m³) for occupational exposure to vinyl chloride, based on the recommendations of the American Conference of Governmental Industrial Hygienists (ACGIH), (Federal Register, May 29, 1971). The ACGIH has since recommended 200 parts per million as a revised voluntary ceiling value for occupational exposure to the chemical. (Documentation of Threshold Limit Values, p. 477).

1973. On May 15, 1973, the Food and Drug Administration published a notice of proposed rule-making for the "prior-sanctioned polyvinyl chloride resin." The notice proposed that the resin not be used as a component of food packaging material for use in contact with alcoholic foods, since both industry and FDA laboratory analyses had found that the vinyl chloride monomer migrates to alcohol from PVC bottles used to package distilled spirits and wine. Analytical results from industry confirmed that levels of up to 20 ppm of vinyl chloride were found to have migrated to the alcohol from the container after it had been stored for up to one year. The FDA concluded: "Vinyl chloride monomer as such is a poisonous and deleterious substance. FDA knows of no studies which establish a safe level of consumption when this monomer is leached from containers into alcoholic foods." (Federal Register, May 15, 1973).

1973. A July 13, 1973, FDA notice in the Federal Register extended the time for filing comments on the FDA proposal for restrictions on polyvinyl chloride packaging, at the request of the plastics industry. The notice stated that the Bureau of Alcohol, Tobacco and Firearms of the Treasury Department (which had first authorized experimental use of PVC bottles for liquor in November, 1968) had terminated the use of PVC containers for alcoholic beverages pending final

action by the FDA on the proposal. As of this date (2/21/74) the Food and Drug Administration has not finalized its proposal of May 17, 1973.

1974. In direct response to the deaths from a rare form of liver cancer of four workers at one polyvinyl chloride plant, the Department of Labor published on January 30, 1974 a request for information and a notice of a fact-finding hearing on the possible hazards associated with the manufacture and/or use of vinyl chloride (Federal Register, January 30, 1974). At the hearing held on February 15, 1974, the Industrial Union Department of the AFL-CIO petitioned for an emergency temporary standard to prevent any worker exposure to vinyl chloride.

VI. The Grave Danger Resulting from Exposure to Vinyl Chloride

A. Acute Effects

Vinyl chloride is a gas which can cause unconsciousness at extremely high concentrations. Inhalation of a 2.5% concentration of vinyl chloride can cause dizziness, disorientation and headache (ILO, p. 1465). At an 8-12% concentration cardiac arrhythmias have been observed in experimental dogs (ACGIH, p. 477). The Committee on Aerosol Toxicity has voiced concern over the use of certain gases--including vinyl chloride--as components of propellant/solvent systems in aerosols because they are capable of producing "cardiac sensitization" (Committee Report, p. 19).

B. Evidence of Carcinogenicity

On January 22, 1974, the B.F. Goodrich Company announced that three--and it is now known five--of its Louisville, Kentucky, vinyl-chloride workers had died of angiosarcoma (or hemangioendothelioma) of the liver, an exceedingly rare form of liver cancer. The five deaths occurred between 1964 and 1973, with the time of development of liver cancer after the onset of exposure to vinyl chloride in the four workers for whom this information is known from 14 to 27 years.

The National Institute for Occupational Safety and Health, estimating that only twenty to thirty people die in the United States every year from this particular type of cancer, has announced the discovery of a new occupational cancer associated with the polymerisation of polyvinyl chloride from vinyl chloride, with vinyl chloride as the chief causative suspect (Statement of Dr. Marcus Key, February 1, 1974). The disease is invariably fatal, once cancer has been initiated (Statement of Dr. Irving Selikoff, February 15, 1974).

The carcinogenic effects of exposure to vinyl chloride have been demonstrated by Viola and Maltoni, in separate experiments. Viola produced angiosarcomas of the liver in rats when exposed to 30,000 ppm for 4 hours/day, 5 days/week, for 12 months (Viola, p. 20). Maltoni has produced the same type of cancers when exposing rats to much lower doses (Statement of Prof. Cesare Maltoni, February 15, 1974). After 127 weeks of exposure to vinyl chloride (4 hours/day; 5 days a week, by inhalation), Maltoni reported liver tumors in Sprague-Dawley rats at exposures as low as 250 ppm. (See table below).

Results of Maltoni's Experimental Study

<u>Exposure level- vinyl chloride, by inhalation</u>	<u># of animals exposed</u>	<u># of animals developing liver angiosarcomas</u>
10,000 ppm	59	6
6,000 ppm	72	11
2,500 ppm	74	9
500 ppm	67	7
250 ppm	67	2
50 ppm	64	0

Dr. Maltoni reported that he is currently conducting an experiment using 300 rats exposed to 50 ppm, since the failure of the low dose of vinyl chloride to induce cancer may be a function of the small number of animals tested.

In addition, Maltoni has observed two fibrosing angiosarcomas in the offspring of pregnant rats exposed to vinyl chloride.

He stated that such fibrosing angiosarcomas have never been observed as occurring spontaneously in Sprague-Dawley rats.

C. Other Evidence of Liver Disease

As early as 1961 Torkelson et al. reported that abnormal histologic changes were noted in the livers of rabbits after repeated exposures to 200 ppm of vinyl chloride. Slight liver enlargement was noted at doses as low as 100 ppm (Torkelson et al.).

A 1967 French study of 160 workers engaged in the production of PVC found liver enlargement in 30% of the cases studied (Suciu et al.).

A later report of the health experience of Dow Chemical's vinyl chloride workers revealed no overt illness, but did determine that certain blood tests of liver function (e.g. beta lipoprotein, the icterus index, and bromosulfalein retention time) were abnormally altered. On the basis of their findings, the authors concluded that some degree of liver dysfunction might result from a TLV for vinyl chloride of 300 ppm (Hutchler et al.).

Marsteller et al. reported within the past few months that 19 out of 20 workers who had been exposed to vinyl chloride for 1-1/2 to 21 years at a PVC producing plant in Germany had some type of liver disease, including gross changes of the liver and spleen. Direct inspection of the liver and spleen (by surgical operation) showed disease to be present in 14 out of the 20 workers (Marsteller et al.).

D. Evidence of Other Chronic Effects

In October 1963 osteolytic lesions were first observed in two Belgian plastics workers who were also suffering from Raynaud's phenomenon due to constriction of the local blood vessels in their hands (ILO, p. 1466). This hand syndrome--termed acroosteolysis--has since been observed in over 30 workers in the United States employed in the manufacture of PVC resins (Wilson et al.).

VII. Relief Requested

21 U.S.C. § 331(a) prohibits the "introduction or delivery for introduction into interstate commerce of any...cosmetic that is adulterated." As defined by 21 U.S.C. § 361(a), a cosmetic is deemed to be adulterated "if it bears or contains any poisonous or deleterious substance which may render it injurious to users..." or "if its container is composed, in whole or in part, of any poisonous or deleterious substance which may render the contents injurious to health." Petitioners seek immediate prohibition of vinyl chloride as a constituent or propellant of aerosolized cosmetics and of polyvinyl chloride as a container for any cosmetic product which can leach out detectable amounts of vinyl chloride from the PVC, because there is substantial evidence that vinyl chloride monomer is carcinogenic. Immediate action is necessary to prevent further human exposure to vinyl chloride monomer.

Respectfully submitted,

Andrea M. Hricko

Sidney H. Wolfe
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2000 P Street, N.W. #703
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Dated: Washington, D.C.
21 February, 1974

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SPECIAL
 DEPARTMENT OF
 HEALTH, EDUCATION, AND WELFARE
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FROM: Hricko, AM & Wolfe, SM (to: Dr. Schmidt)			CONTROL NO. HF-3635
SUBJECT AND DATE: Ltr-2/21/74-re rising number of cases of liver cancer in workers exposed to vinyl Chloride.			DATE REC'D. 2/22/74
			DUE DATE
REFERRED (1) HFC-10	(2) 2-22-74 HFC-20	(3)	(4)
DATE: 2/22/74			
REPLY SENT TO: for direct action			DATE RELEASED
REMARKS Dr. Schmidt, Mr. Gardner -- info			ACKNOWLEDGED-DATE <input type="checkbox"/>
			NO ANSWER NEEDED <input type="checkbox"/> (EXPLAIN IN REM'KS)

HEW-73
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